REMARKS AND ARGUMENTS

I. The Information Disclosure Statement

At page 2 of the office action, the Examiner informs Applicants that the references cited in the submitted Search Report were not considered allegedly because the submission of the Information Disclosure Statement did non comply with 37 CFR 1.98 in that that no copies of references were submitted with the disclosure. In response, Applicants bring to the Examiner's attention that 37 CFR §1.98(d) states as follows:

> (d) A copy of any patent, publication, pending U.S. application or other information, as specified in paragraph (a) of this section, listed in an information disclosure statement is required to be provided, even if the patent, publication, pending U.S. application or other information was previously submitted to, or cited by, the Office in an earlier application, unless:
>
> (1) The earlier application is properly identified in the information disclosure statement and is relied on for an earlier effective filing date under 35 U.S.C. 120; and
>
> (2) The information disclosure statement submitted in the earlier application complies with paragraphs (a) through (c) of this section.

Accordingly, Applicants respectfully submit that copies of the references listed on the Information Disclosure Statement at issue were submitted and considered during the prosecution of the parent application, U.S. Patent Application No. 09/726,219 (now U.S. Patent No. 6,806,079) from which the above-identified patent application claims its priority.

II. Drawings

At page 3 of the Office action the Examiner objected to drawings previously submitted by Applicants because tables and sequence listing included in the specification must not be duplicated in the drawings. The Examiner then suggested that Applicants should amend the specification by deleting any figures/drawings which consist only of nucleic acid or protein sequences which would be submitted in their entirety in computer readable format and should further amend the specification accordingly to reflect the replacement of the drawings/figure by the appropriate SEQ ID No. The Examiner suggested in alternative that if a drawing provides additional information not provided in the sequence listing, then the drawing may remain with an appropriate SEQ ID No. for each sequence.

In reviewing 52 figures submitted for the above-identified patent application, Applicants find that if there is a sequence listed on any of the drawings, the sequence is accompanied by an appropriate SEQ ID No. Applicants also find that if a Figure depicts a sequence, the Figure provides additional information which would not be available from the sequence listing. For example, Figure 4 discloses restriction enzyme sites and general alignment of the sequences within Gene III; Figure 5A lists restriction enzyme sites, location of pelB leader and location of linker peptide; shows alignment of Myc TAG; Figure 8 maps a cleavage site and restriction sites; Figure 10 discloses alignment of amino acid sequences with corresponding DNA sequences; Figure 13 provides an alignment and also lists restriction sites; Figure 15 discloses 4 different alignments; Figure 16 provides different alignments and information about these alignments would be lost if we were to delete the Figure and rely on the information disclosure only; Figure 24

discloses a wealth of information, such as location of CDR1, CDR2 and CDR3 regions, all of which would be lost if Applicants were to delete the Figure. The same rational applies to the rest of the Figures submitted for the above-identified patent application.

In conclusion, each of the Figures submitted for the above-identified patent application contains alignment and mapping information that would be lost if Applicants were to delete the Figures and rely on the submitted sequence listing only.

III. Objections to Applicants' Specification Should Be Withdrawn

At page 4 of the Office action, the Examiner objected to Applicants' specification because the abstract of disclosure contains more than 150 words. In response, Applicants submit an amended abstract with this response. As amended, the Abstract contains less than 150 words and therefore, complies with the requirements of the MPEP §608.01.

At page 4 of the Office action, the Examiner also objected to the specification because some sequences listed in the specification, do not contain corresponding SEQ ID Nos. In response, Applicants submit herewith amendments to the specification in which SEQ ID NOs are presented for each of the sequences. Applicants also submit amendments to the specification in which symbols "^{0}C" are corrected.

IV. Patentability Arguments

A. The Claim Rejections Under 35 USC §112, First Paragraph, Should Be Withdrawn

At page 5 of the Office action, the Examiner rejected claims 1-5 because according to the Examiner, the claims contain subject matter which was not described in

the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor had possession of the claimed invention. Specifically, the Examiner argues that "the claimed invention states that the binding molecule has a "desired specificity" for the target. However, the claims of invention do not include any structural information regarding how the binding molecule binds the target or a binding affinity range that would be considered 'desired specificity.'"

The specification as filed, beginning in line 27 of page 28 provides:

> This describes a pair of molecules (each being a member of a specific binding pair) which are naturally derived or synthetically produced. One of the pair of molecules, has an area on its surface, or a cavity which *specifically binds* to, and is therefore defined as complementary with a particular spatial and polar organisation of the other molecule, so that the pair have the property of *binding specifically* to each other. Examples of types of specific binding pairs are antigen-antibody, biotin-avidin, hormone-hormone receptor, receptor-ligand, enzyme-substrate, lgG-protein A.

Thus, the specification clearly describes what constitutes specific binding by describing specific binding and by giving examples of binding pair members having a "desired specificity."

The specification then discloses specific examples in which specific binding pair members with various desired specificities were described (see examples 4, 6, 43, 45 and 46).

Thus, the specification as filed provides a written description for isolating binding molecules with a sought-after (desired) specificity. Consequently, the term "desired specificity" is described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the application was filed, had possession of the claimed invention. Thus, the rejection under 112, first paragraph, over

the use of the term "desired specificity" in the claims can be properly withdrawn and such withdrawal is respectfully requested herein.

At page 6 of the Office action the Examiner issued another written description rejection which, according to the Examiner, was made because one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed since the structural limitation of the nucleic acid necessary for surface display is not included in the claimed invention. The Examiner believes that the specification does not teach how every known and every potential "binding molecules" of every size and structure can be surface displayed on every filamentous bacteriophage. In support of this conclusion, the Examiner cites *Fiddes v. Baird*, in which claims directed to mammalian FGF's were found unpatentable due to lack of written support for the broad class wherein the specification provided only the bovine sequence.

Applicants bring to the Examiner's attention that in *Ex parte Neuberger and Rabbitts* (a copy of which is enclosed with this response for Examiner's convenience as Exhibit A), one of the issues before the Board of Patent Appeals and Interferences was whether claim 42 (directed to a method for the production of a chimeric antibody) was properly rejected under 35 USC §112. The *Ex parte Neuberger* Examiner rejected claim 42 because he believed that "disclosure of thee functional chimeric antibodies is insufficient evidence to support the present claims as all chimeric antibodies prepared from all non-Ig proteins as being functional." The Board of Appeals disagreed and concluded that Examiner's argument was not persuasive and that the presence of the three functional examples was sufficient to support the scope of a method claim.

Applicants submit further that the specification discloses a range of working examples of various types of binding molecules that folded correctly so as to be able to bind the complementary target (antigen for the different antibody molecules, substrate for enzyme, ligand for receptor). Specifically, the specification provides the following examples of proteins that have been displayed on filamentous phage using the claimed methods:

- antibody dAb molecule, VH domain (single domain forms binding site) – Example 4;
- antibody scFv molecule (two domains cooperate to form binding site) – at least Examples 4, 6, 8, 9, 13, 18, 21, 23, 25, 29, 43 and 45;
- platelet-derived growth factor receptor (PDGF-R, a monomeric binding protein) – Examples 15 and 16;
- staphylococcal nuclease (a monomeric enzyme) – Example 36;
- amino-terminal domains of human CD4 (monomeric receptor) – Example 37;
- antibody Fab fragments (two-chain molecules, cooperate to form binding site) – at least Examples 7, 25, 26, 27, 33 and 41;
- antibody Fv fragments (another two-chain molecule, cooperating to form binding site) – at least Example 39;
- alkaline phosphatase (only enzymatically active as a dimer – experiments show enzyme activity, which requires binding) – Examples 11, 12, 30, 31 and 32.

Thus, the specification demonstrates that a wide variety of functional and structurally different proteins can be displayed according to the claimed methods such that they are able to bind a relevant complementary specific binding pair member.

Because Applicants clearly demonstrate in their specification that their methods can be practiced with a variety of proteins, Applicants submit that they were in possession of

the methods as presently claimed at the time of filing and, therefore, that the rejections should be withdrawn.

At page 6 of the Office action, the Examiner also takes issue with the limitation "filamentous phage" and concedes that the specification teaches M13 and fd as the examples of filamentous bacteriophages. The Examiner then concludes that despite the examples, Applicants' assertion that any filamentous bacteriophage can be used in the instant methods is simply recitation of a "laundry list" of other bacteriophages further citing MPEP 2163.05 which provides

> A lack of adequate written description issue also arises if the knowledge and level of skill in the art would not permit one skilled in the art to immediately envisage the product claimed from the disclosed process. See, e.g., *Fujikawa v. Wattanasin*, 93 F.3d 1559, 1571, 39 USPQ2d 1895, 1905 (Fed. Cir. 1996) (a "laundry list" disclosure of every possible moiety does not constitute a written description of every species in a genus because it would not "reasonably lead" those skilled in the art to any particular species).

However, Applicants submit that unlike a laundry list of any known bacteriophages, the instant claims are supported by recitation of a clearly defined genus of filamentous bacteriophages, several members of which were used in working examples in the specification as filed. Filamentous bacteriophages are a particular family of bacteoriophages which share several important characteristics: they are secreted, they are filamentous, they share similar structures and similar genomes. Page 4.3 of Sambrook (on the record with the US PTO) confirms that the filamentous phages f1, fd and M13 are so similar as to be essentially identical.

The Examiner also concedes that the specification teaches that the nucleic acids for gIII and gVIII genes of filamentous bacteriophages can be utilized to display a binding member on the bacteriophage surface according the claimed methods.

Nevertheless, the Examiner concludes that "one skilled in the relevant art would not reasonably conclude that Applicants had possession of the invention as claimed since the structural limitation of the nucleic acid necessary for surface display is not included in the claimed invention.

Pending claim 1 of the instant application recites a limitation to "wherein each filamentous bacteriophage particle contains a phagemid genome comprising nucleic acid with a nucleotide sequence encoding the binding molecule expressed from the nucleic acid and displayed by the particle at its surface."

Furthermore, Applicants amend with this response instant claim 1 by reciting a limitation "and wherein a helper phage, or a plasmid expressing complementing phage genes, is used to package said phagemid genome within each filamentous bacteriophage particle."

These limitations clearly provide that the instant claims recite a limitation to filamentous bacteriophage genes for packaging nucleic acid in the bacteriophage and displaying a binding member on the surface of a bacteoriophage. Thus, the structural limitation of the nucleic acid necessary for surface display is included in the claimed invention and therefore, the instant invention is clearly defined.

In conclusion, for the reasons discussed above, Applicants submit that the present application fully complies with 35 USC §112; and withdrawal of the rejection is respectfully requested.

B. The Claim Rejections Under 35 USC §102 Should Be Withdrawn

At page 7 of the Office action, the Examiner rejected claims 1-5 as being anticipated by Ladner et al. U.S. Patent 5,223,409 (Ladner et al.). The Examiner alleges that Ladner et al. anticipates the instant claims because it teaches methods of displaying binding proteins on the surface of filamentous bacteriophage via nucleic acid sequences including gIII and screening for target molecule binding.

Applicants amend the instant claims with this response for clarification purposes by adding the following language: "wherein a helper phage, or a plasmid expressing complementing phage genes, is used to package said phagemid genome within each filamentous bacteriophage particle." The Ladner method does not utilize a helper phage or a plasmid expressing complementing phage genes and therefore, Ladner et al cannot anticipate the currently amended claims as a matter of law.

This amendment does not introduce any new matter and is fully supported by the specification as filed, e.g. examples 17, 18, 19, 24, 25, 26, 27, 34, 42, 43 and 44.

In conclusion, because Ladner et al. does not utilize a helper phage in its methods, Ladner et al. cannot anticipate the instant claims under 35 USC §102 as a matter of law. Therefore, the Examiner may properly withdraw the rejection of Applicants' claims over Ladner et al. and such withdrawal is respectfully requested.

C. Double Patenting Rejections are Moot and Should Be Withdrawn

At pages 8 through 12 of the Office action, the Examiner rejected claims 1 to 5 under the doctrine of non-statutory double patenting over co-owned US patents 5,969,108; 5,885,793; 6,555,313 and 6,582,915. In response, Applicants file a terminal disclaimer with this response that disclaims any part of term granted on the instant

application beyond the term of co-owned U.S. Patent Nos: 5,969,108; 5,885,793; 6,555,313 and 6,582,915.

Applicants believe that the terminal disclaimer overcomes rejection of the instant claims over co-owned US patents 5,969,108; 5,885,793; 6,555,313 and 6,582,915 and request that the Examiner withdraw the rejection.

At page 12 of the Office action, the Examiner listed other patents co-owned by Applicants, such as 5,871,907; 5,858,657; 5,837,242; 7,063,943; 6,916,605; 6,521,404; 6,544,731 and 6,593,081. The Examiner then asserted that she rejected the pending claims under the doctrine of non-statutory double patenting over these patents. Applicants submit a terminal disclaimer with this response disclaiming any portion of the patent term to be granted on the above-identified patent application that would exceed the patent term for 5,871,907; 5,858,657; 5,837,242; 7,063,943; 6,916,605; 6,521,404; 6,544,731 and 6,593,081.

In conclusion, because of the enclosed herewith terminal disclaimer, the rejection of Applicants' claims over 5,871,907; 5,858,657; 5,837,242; 7,063,943; 6,916,605; 6,521,404; 6,544,731 and 6,593,081 may be properly withdrawn and such withdrawal is requested herein.

CONCLUSION

Applicants believe that the application is in good and proper order for allowance and such allowance is respectfully solicited. The Examiner is hereby respectfully invited to contact the undersigned attorney at the number listed below with any questions, comments or suggestions relating to this application. Should any additional fees be required for further prosecution of the above-identified patent application, the Commissioner is authorized to deduct any such fees from Howrey LLP Deposit Account No. 08-3038, referencing the above-identified docket number.

Respectfully submitted,
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